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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/658,989	09/10/2003	Jan Bastiaan Bouwstra	BOUWSTRA-3	6068

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EXAMINER	
DESAI, ANAND U	
ART UNIT	PAPER NUMBER
1653	

DATE MAILED: 01/24/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/658,989	BOUWSTRA ET AL.	
	Examiner	Art Unit	
	Anand U. Desai, Ph.D.	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 October 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-28,31 and 32* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-28,31 and 32* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *20051222*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. This office action is in response to Amendment filed on October 27, 2005. Claims 1-28, 31, and 32 are currently pending and are under examination.

Withdrawal of Rejections

2. The rejection of claims 5, 7, 13, 20, and 22 under 35 U.S.C. 112, second paragraph as being indefinite is withdrawn.

3. The rejection of claims 1-28, 31, and 32 under 35 U.S.C. 103(a) as being unpatentable over Chang, C. et al. (WO 01/34646 A2) in view of Olsen et al. U.S. 6,413,742 B1 is withdrawn.

Information Disclosure Statement

4. The information disclosure statement filed December 22, 2005 fails to comply with 37 CFR 1.98(a)(2), which requires a legible copy of each cited foreign patent document; each non-patent literature publication or that portion which caused it to be listed; and all other information or that portion which caused it to be listed. It has been placed in the application file, but the information referred to therein has not been considered. The reference does not contain all of the pages.

Claim Objections

5. Claim 13 is objected to because of the following informalities:

There is a typographical error. There appears to be an inadvertent separation placed in the word, "residue" on the third line.

Appropriate correction is required.

Maintenance of Rejections

Double Patenting

6. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., In re Berg, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); In re Goodman, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); In re Longi, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); In re Van Ornum, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); In re Vogel, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and In re Thorington, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

7. Claims 1-28, 31, and 32 stand provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-20 of copending application No. 10/469,747 (U.S. Patent Application Publication 2005/0119170 A1). The rejection was disclosed in the office action mailed June 24, 2005.

Response to Remarks

Applicant states the claims of the present application are believed clearly and patentably distinguished from the claims of copending application number 10/469,747. The claims of 10/469,747 are directed to a plasma substance composition, and its use as a plasma expander, in which less than 2% of the amino acid residues in the gelatin-like protein are hydroxyproline residues. Applicant states the invention claimed in copending application 10/469,747 can reduce

the risk of immunological reactions. Applicant states the claims of the pending application are limited to a composition or method of providing same comprising a recombinant gelatin-like protein having an isoelectric point less than 8, which solves the problem in the art of unduly rapid blood clearance rates. Applicant states the claims of the copending application do not remotely suggest that the problem in the art of unduly rapid blood clearance rates can be solved by a recombinant gelatin-like protein having an isoelectric point less than 8.

Applicant's arguments have been fully considered but they are not persuasive. The copending application does claim a composition comprising a solution of saline in a physiologically acceptable concentration and a protein having a colloid osmotic function, wherein the protein having the colloid osmotic function is a recombinant gelatin-like protein comprising Gly-Xaa-Yaa triplets in which less than 2% of the amino acid residues are hydroxyproline residues, with a molecular weight of at least 10,000 Daltons. The composition can be used as a plasma expander (see claims 1, 7, and 15). In addition, paragraph [0030] of copending application 10/469,747 states "the clearance speed of the gelatin-like proteins can be designed-in by the choice for a or size or a specific range of sizes of the gelatin-like proteins....Yet further the isoelectric point can be tuned by the composition of acidic and basic amino acid residues in the gelatin-like proteins". Paragraph [0067] describes a gelatin-like protein (Biogel II) with a molecular weight of 15.1 kDa, and an isoelectric point of 5.1 that would be one of the recombinant gelatin-like proteins with colloid osmotic function. Therefore, a person having ordinary skill in the art would have expected the composition disclosed in the copending application to function as a plasma substitute composition having a low blood clearance, because the copending specification describes a species of a recombinant gelatin-like

protein that is meant to function as a protein with colloid osmotic function for use as a plasma expander, which has a molecular weight of at least 10,000 Daltons and an isoelectric point of less than 8.0.

Claim Rejections - 35 USC § 112

8. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

9. Claims 1-7, 9-14, 18-22, 24-27, and 31-32 stand rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The rejection was disclosed in the office action mailed June 24, 2005.

Response to Remarks

Applicant states the claims are limited to the presence in the recited recombinant gelatin-like protein of the distinctive Gly-Xaa-Yaa triplets, which are characteristic of gelatin, and gelatin-like proteins. Applicant states possession of the claimed invention by directing attention to the specification, which describes the structure of peptides referencing the MW of the monomer, the Gly-Xaa-Yaa motif, and the isoelectric point. Applicant cites as example, figure 3, to demonstrate that any amino acid can be altered as long as the peptide retains the claimed molecular weight of the monomer and an isoelectric point below 8. Figure 3 is stated to show an increase in duration of the hyperoncotic effect by reducing the isoelectric point from above 8 to below 8 (pI 4.6, for the modified tetramer peptide sequence identified as SEQ ID NO: 4). Applicant cites pages 5, lines 11-17, and lines 23-32, page 7, line 27 to page 8, line 20, and the whole of page 10 to provide further evidence of possession of the invention as claimed.

Applicant's arguments have been fully considered but they are not persuasive. In response to applicant's argument, it is noted that the feature upon which applicant relies (i.e., a recombinant gelatin-like protein comprising Gly-Xaa-Yaa triplets) is not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

The term recombinant gelatin-like protein is being reasonably interpreted to be any amino acid sequence that would retain a molecular weight of at least 10,000 Daltons to at most 50,000 Daltons, and that has an isoelectric point of less than 8. As applicant stated, "any amino acid may be altered as long as the peptide retains the claimed molecular weight of the monomer and an isoelectric point below 8", and therefore the breath and scope of the recombinant gelatin-like protein is not described by a precise protein structure and/or polypeptide sequence.

The MPEP states that the purpose of the written description requirement is to ensure that the inventor had possession, at the time the invention was made, of the specific subject matter claimed. The courts have stated:

> "To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." *Lockwood v. American Airlines, Inc.*, 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (Fed. Cir. 1997); *In re Gostelli*, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) ("[T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." *Lockwood*, 107 F.3d at 1572, 41 USPQ2d at 1966." *Regents of the University of California v. Eli Lilly & Co.*, 43 USPQ2d 1398.

Further, for a broad generic claim, the specification must provide adequate written description to identify the genus of the claim. In *Regents of the University of California v. Eli Lilly & Co.* the court stated:

> "A written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." *Fiers*, 984 F.2d at 1171, 25 USPQ2d 1601; *In re Smythe*, 480 F.2d 1376, 1383, 178 USPQ 279, 284985 (CCPA 1973) ("In other cases, particularly but not necessarily, chemical cases, where there is unpredictability in performance of certain species or subcombinations other than those specifically enumerated, one skilled in the art may be found not to have been placed in possession of a genus ...") *Regents of the University of California v. Eli Lilly & Co.*, 43 USPQ2d 1398.

MPEP § 2163 further states that if a biomolecule is described only by a functional characteristic, without any disclosed correlation between function and structure of the sequence, it is "not sufficient characteristic for written description purposes, even when accompanied by a method of obtaining the claimed sequence." MPEP § 2163 does state that for a generic claim the genus can be adequately described if the disclosure presents a sufficient number of representative species that encompass the genus. If the genus has a substantial variance, the disclosure must describe a sufficient variety of species to reflect the variation within that genus. See MPEP § 2163. Although the MPEP does not define what constitute a sufficient number of representative species, the courts have indicated what do not constitute a representative number of species to adequately describe a broad generic. In *Gostelli*, the courts determined that the disclosure of two chemical compounds within a subgenus did not describe that subgenus. *In re Gostelli*, 872, F.2d at 1012, 10 USPQ2d at 1618.

The factors considered in the Written Description requirement are (1) *level of skill and knowledge in the art*, (2) *partial structure*, (3) *physical and/or chemical properties*, (4)

functional characteristics alone or coupled with a known or disclosed correlation between structure and function, and the (5) *method of making the claimed invention.* Disclosure of any combination of such identifying characteristics that distinguish the claimed invention from other materials and would lead one of skill in the art to the conclusion that the applicant was in possession of the claimed species is sufficient." MPEP § 2163.

In the instant case, the claims are drawn to composition comprising a recombinant gelatin-like protein with a molecular weight of from at least 10,000 Daltons to at most 50,000 Daltons that has an isoelectric point of less than 8 and is not crosslinked by chemical modification, which has colloid osmotic function.

(1) Level of skill and knowledge in the art:

The level of skill and knowledge required in the art to manufacture a plasma substitute composition comprising a gelatin-like protein having a low blood clearance rate is high, and typically that of a doctoral scientist with several years of experience.

(2) Partial structure:/ (3) Physical and/or chemical properties: / (4) Functional characteristics:

The specification discloses the use of recombinant gelatin-like polypeptide identified as SEQ ID NO: 1 with a MW of 18.4 kDa and an isoelectric point of 5.35, a trimer of SEQ ID NO: 1 (SEQ ID NO: 2), a tetramer of SEQ ID NO: 1 (SEQ ID NO: 3), and a modified version of SEQ ID NO: 1, wherein the glutamine residues were replaced by glutamic acid residues and asparagine residues were replaced by aspartic acid residues to reduce the isoelectric point from 8.7 to 4.6 (SEQ ID NO: 4) that are used to demonstrate an increase in duration of the increased oncotic pressure. The gelatin-like polypeptides were used in a radio allergen sorbent test to determine the risk of immunological reaction to the administration of gelatin-like polypeptides.

The sequences identified as SEQ ID NO: 2, 3, and 4 did not elicit an immune reaction (page 27, Results table).

(5) Method of making the claimed invention:

Gelatin-like polypeptides were produced by recombinant methods as disclosed by EP-A-0926543 or EP-A-1014176; Both citations describe the recombinant expression in yeast, *Pichia patoris*, where the gelatin-like nucleic acid sequence is designed based on codon usage in *Pichia patoris*.

As stated *supra*, the MPEP states that written description for a genus can be achieved by a representative number of species within a broad genus. The claims are drawn to any recombinant gelatin-like protein that encompasses any amino acid that may be altered as long as the peptide retains the claimed molecular weight of the monomer and an isoelectric point below 8. The possible variations are enormous. Since the MPEP states that if a biomolecule is described only by a functional characteristic, without any disclosed correlation between function and structure, it is "not sufficient characteristic for written description purposes, even when accompanied by a method of obtaining the claimed sequence." MPEP § 2163. Here, though the claims may recite some functional characteristics, the claims lack written description because there is no disclosure of a correlation between function and structure of the recombinant gelatin-like polypeptide sequences beyond those disclosed in the examples in the specification. Moreover, the specification lacks sufficient variety of species to reflect this variance in the genus since the specification does not provide any examples of any other amino acid modifications of gelatin protein sequences.

While having written description of a recombinant gelatin-like protein comprising SEQ ID NO: 1, and modified SEQ ID NO: 1 as disclosed as SEQ ID NO: 4, identified in the

specification and examples, the specification is devoid of any other modified gelatin-like polypeptide sequence that qualify for the functional characteristics claimed.

The description requirement of the patent statue requires a description of an invention, not an indication of a result that one might achieve if one made that invention. See *In re Wilder*, 736, F.2d 1516, 1521, 222 USPQ 369, 372-73 (Fed. Cir. 1984) (affirming rejection because the specification does "little more than outlin[e] goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate.") Accordingly, it is deemed that the specification fails to provide adequate written description for the genus of the claims and does not reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the entire scope of the claimed invention.

Conclusion

10. No claims are allowed.

11. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anand U. Desai, Ph.D. whose telephone number is (571) 272-0947. The examiner can normally be reached on Monday - Friday 7:00 a.m. - 3:30 p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon P. Weber can be reached on (517) 272-0925. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

January 16, 2006

JON WEBER
SUPERVISORY PATENT EXAMINER